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Priming effect of a birch pollen season studied with laser Doppler flowmetry in patients with allergic rhinitis

S. JULIUSSON *and* M. BENDE

Department of Otolaryngology, Central Hospital, Skövde, Sweden

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Summary

Nasal mucosal provocation tests were done on eight patients with seasonal allergic rhinitis before and after a birch pollen season. The effects on nasal microvascular blood flow were detected by means of laser Doppler flowmetry. The patients reacted to the birch pollen provocation with an increase in blood flow. This increase was greater after the pollen season than before, when the same pollen doses were used, indicating a priming phenomenon of the resistance vessels.

Introduction

The pathophysiology of the allergic reaction is complex, and the subjective and objective effects are results of an uncontrolled pool-reaction of the involved mediators. Little is known about the mechanisms responsible for the changes in a patient's reactivity from one day to another or between successive years. In 1968 Connell [1] found that challenges with ragweed pollen given daily for 1 hr on 4 successive days decreased the nasal threshold for allergic rhinitis more than five-fold, a phenomenon he called 'the priming of the end organ'. He also found that environmental exposure during a ragweed pollen season primed ragweed-sensitive individuals.

In a previous study we reported how laser Doppler flowmetry can be used to detect changes in nasal microvascular blood flow after challenge with birch pollen in sensitized patients with seasonal allergic rhinitis [2].

The aim of the present investigation was to study whether the pollen season changes the reactivity of the nasal mucosal microvascular bed in patients with seasonal allergic rhinitis.

Patients and methods

Eight patients (six men and two women, aged 20–29 years) voluntarily entered the study and gave informed consent. All were asymptomatic at the start of the study but had a history of hypersensitivity to birch pollen, which was confirmed by positive skin-

Correspondence: Mats Bende, MD, Department of Otolaryngology, Central Hospital, S-541 85 Skövde, Sweden.

prick test and allergen-challenge test. None was on any medication with known influence on the nasal mucosa.

The measurements were performed 2 weeks before and in the second week after the birch pollen season, which, in this part of Sweden, usually starts in the second week of May and lasts for 3–4 weeks. The only medications that the patients received during the study were oral or topical nasal decongestants (phenylpropanolamine or xylometazoline) for occasional use in case of severe nasal blockage.

The microcirculation of the nasal mucosa was investigated by means of a laser Doppler flowmeter (Periflux, PF 1d, Perimed, Sweden) as described previously [2]. The tip of the probe was fixed under visual guidance in a position close to the mucosal surface of the anterior part of the inferior turbinate. The laser Doppler signal is known to be stable at a distance between probe and mucosa up to 3–5 mm [3]. The probe was checked frequently during tests and minimally adjusted if necessary.

The allergen provocations were performed by topical application of 0·05 ml test solution with a micropipette on the nasal mucosa in front of the laser Doppler probe. Test solutions used were a purified aqueous birch pollen extract (Pharmalgen, Pharmacia, Uppsala, Sweden), in serial dilutions of 50–100 000 BU/ml (biological units), and the diluent; administered at room temperature (20 °C) and stored at 6 °C. Before each experiment the patient rested in the supine position for 10 min, whereafter the series of challenges commenced with the diluent (placebo) and then the first provocation was performed with dose a. Each patient's allergic history and reactions to previous provocations were taken into account and an individual pollen dose was chosen to give only slight symptoms. After a 15–30 min break, a second provocation was done with dose b ($b = 10 \times a$). The birch pollen concentration in dose a was in the dilutions of 50–10 000 BU/ml and that of dose b in the dilutions of 500–100 000 BU/ml. A 5-min stable registration before every application was required to give a baseline value [2]. The registration after each application was observed for 15 min. Thus, for every patient the effect of placebo, dose a and dose b before and after the pollen season was studied.

Statistics

Blood-flow values every thirtieth second were extracted from the registrations and used in the calculations. The area under the curve (AUC) in percentage of baseline value was used in the comparisons. The statistical analyses were performed with Student's paired *t*-test.

Results

When asked after the pollen season the patients replied that their nasal symptoms during the pollen season had been moderate and that they had used medications sparingly. At the time of the post-seasonal provocation the patients had not been on medication for at least 24 hr. The patients responded to the provocations with nasal symptoms such as itching and the urge to sneeze associated with the pollen dose. Blood flow increased after pollen provocation in a dose-dependent manner before as well as after the season (Fig. 1). After the pollen season the provocation increased the blood flow more than before the season, with the same doses ($P = 0{\cdot}10$ and $P = 0{\cdot}03$ for doses a and b, respectively).

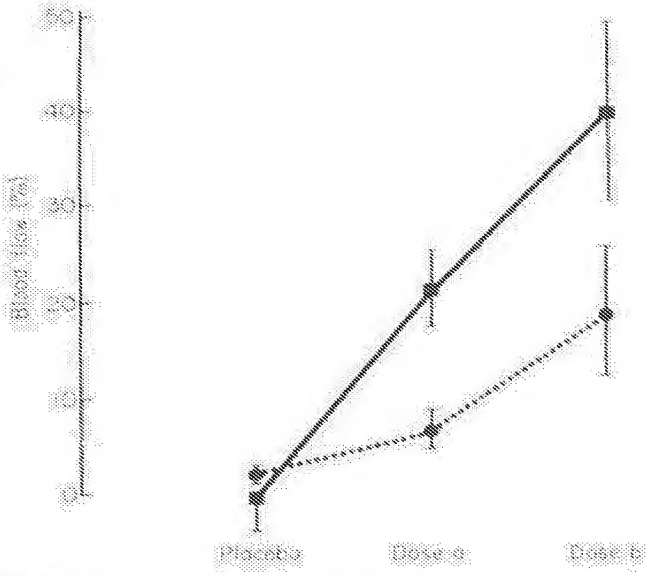

Fig. 1. The effect on nasal mucosal blood flow (mean ± S.E.) after pollen dose a and dose b compared with placebo in provocation tests in eight patients with seasonal allergic rhinitis before (●) and after (■) the pollen season.

Discussion

Connell [1] defined the priming effect as an increase in reactivity of the nasal membrane following repeated exposure to pollen. He measured nasal patency and observed changes in nasal reactivity during and after a pollen season. Changes in nasal patency are dependent on the state of the capacitance vessels and the degree of oedema in the tissue.

In contrast to studies of nasal patency, laser Doppler flowmetry detects changes in the microcirculation, a parameter that is independent of the state of the capacitance vessels. The blood flow and the blood content of the human nasal mucosa are regulated by different mechanisms [4,5]. The effect of an increased blood flow after pollen provocation in this study is in accordance with our previous findings that were measured with the laser Doppler flowmeter [2], but it is in contrast to the results as measured with the 133-Xe washout technique [6]. This difference is probably due to the fact that the two methods measure the blood flow in different parts of the nasal mucosa. The 133-Xe washout method assesses the mean perfusion and the laser Doppler flowmeter reflects the superficial blood flow [7]. The effect of an increased reactivity after the pollen season indicates that the priming phenomenon also induces effects on the microvascular bed.

The effect of nasal decongestants like xylometazoline is to reduce blood flow [7]. The duration of the effect is less than 12 hr so occasional treatment during the pollen period should not interfere with the results of the provocations.

The hyperreactivity found in the nasal challenge models is not only an increased sensitivity to released mediators but also an increased mediator release from nasal mucosal mast cells and basophils [8]. The absolute and relative number of nasal mucous membrane mast cells is significantly increased during the pollen season, compared with numbers at other times [9]. The nature of the increased responsiveness

is not clear, but it is transient and reproducible, and appears to be an immunological phenomenon because neither ammonia, histamine nor metacholine dose appear to induce any nasal hyperreactivity [10,11].

The clinical implication is that the allergic reaction increases the blood flow as detected with laser Doppler flowmetry and the priming effect causes an increased sensitivity of the resistance vessels.

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